

REMARKS

Claims 1-52 are pending in the application. Claims 24-43 have been withdrawn as being drawn to a non-elected invention. Accordingly, claims 1-23 and 44-52 are under examination. Applicants have reviewed the rejections set forth in the Office Action mailed September 28, 2004, and respectfully traverse all grounds for the reasons that follow.

Rejections Under 35 U.S.C. § 102

Claims 1 and 4-8 stand rejected under 35 U.S.C. § 102(a) as anticipated by Masselon et al. allegedly because Masselon et al. describes identifying polypeptides in a sample mixture where the mass of a sample is compared to the mass of a database. The Office alleges that the generation of a list of all possible tryptic fragment masses corresponds to an empirically determined characteristic and that such list is compared to a list of parent ion masses to create an annotated polypeptide index. The Office further asserts that the declaration submitted by Dr. Camp is inadequate allegedly because it fails to provide factual supporting evidence.

Claim 1 is directed to a method for identifying a polypeptide. The method includes determining two or more characteristics associated with the polypeptide where one characteristic is the mass of a peptide fragment determined by mass spectrometry. The two or more characteristics are compared to an annotated polypeptide index having at least one empirically determined characteristic for each of the polypeptides in the index to identify one or more polypeptides in the annotated polypeptide index having the two or more characteristics.

When lack of novelty is based on a printed publication that is asserted to describe the same invention, a finding of anticipation requires that the publication describe all of the elements of the claims. *C.R. Bard, Inc. v. M3 Sys., Inc.*, 157 F.3d 1340, 1349, 48 U.S.P.Q.2d 1225, (Fed. Cir. 1998) (quoting *Shearing v. Iolab Corp.*, 975 F.2d 1541, 1544-45, 24 U.S.P.Q.2d 1133, 1136 (Fed. Cir. 1992)). To establish a *prima facie* case of anticipation, the Office must show that the single reference cited as anticipatory art describes all the elements of the claimed invention.

The Office fails to particularly point out each of the elements claimed by in the invention that are allegedly described in Masselon et al. Instead, the Office appears to provide a

conclusory statement asserting that the cited reference anticipates the claimed invention and cursorily finds the declaration by Dr. Camp inadequate. Several passages are generally pointed to in the Office Action as allegedly describing the recited elements of the claimed invention. However, none of the passages cited in Masselon et al. describe the invention as claimed.

Regarding the declaration by Dr. Camp, Applicants draw the Office's attention to the fact that the declaration was submitted under 37 C.F.R. § 1.132, not § 1.131, as an opinion by an expert in the field of proteomics and mass spectrometry. Such opinion testimony should be accorded its proper weight and given deference by the Office. Further, the submitted declaration did set forth a basis for Dr. Camp's opinion that Masselon et al. did not describe the claimed invention. In particular, Dr. Camp stated:

With regard to Masselon et al., this reference compares peptides analyzed by mass spectrometry (MS) to a database generated by *in silico* trypsin digestion of *Caenorhabditis elegans* genomic sequence.

Camp Declaration at paragraph 5 (emphasis added).

The reference to *in silico* generation of the trypsin digested peptides refers to the process of computer generating the predicted peptides. Therefore, the declaration sufficiently shows that the tryptic peptides were not empirically determined.

Further, the plain language of the claim requires that the claimed annotated polypeptide index contain at least one empirically determined characteristic for each of the polypeptides in the index. Masselon et al. fails to describe an empirically determined characteristic for the described computer generated fragments.

The term "empirical" means "originating in or relying or based on factual information, observation, or direct sense experience usually as opposed to theoretical knowledge." *Webster's Third New International Dictionary, Unabridged*. Merriam-Webster, 2002. <http://unabridged.merriam-webster.com> (20 Mar. 2005). The tryptic fragments described by Masselon et al. and cited by the Office are not empirically determined. Such peptides are theoretically derived because they are predicted by a computer from an amino acid sequence and

forecast all possible fragments that can arise from a particular sequence. Masselon et al. describe the theoretical nature of the predicted tryptic peptides when the reference describes:

In this initial work, the sequences for the set of model polypeptides selected for study were added to the full database of predicted polypeptides that could be produced by enzymatic digestion of proteins for *C. elegans*. The predicted polypeptides included all possible species from incomplete digestion, and studies also included the generation and use of modified polypeptide libraries.

Masselon et al., page 1922, Figure 3 legend (emphasis added).

Because the tryptic peptides of Masselon et al. are predicted and not based on factual information, observation, or direct sense experience and amount to theoretical knowledge. Theoretical knowledge does not constitute an empirical characteristic as claimed. Therefore, Masselon et al. does not describe an annotated polypeptide index containing at least one empirically determined characteristic for each of the polypeptides in the index. Withdrawal of this ground of rejection is respectfully requested.

Claims 1, 2, 8-12 and 50 stand rejected under 35 U.S.C. § 102(b) as anticipated by Yates. The Office alleges that Yates describes mass mapping where a determined mass of a polypeptide is compared with database information of another organism to identify the polypeptide. The Office also alleges that Yates describes shotgun identification of digested proteins in mixtures where the masses of a protein fragments are compared using a computer algorithm and database to reconstruct the identities of the proteins. The Office further asserts that the declaration submitted by Dr. Camp is inadequate allegedly because it fails to provide factual supporting evidence.

Claim 1 is directed to a method for identifying a polypeptide that includes comparing two or more characteristics associated with a polypeptide to an annotated polypeptide index having at least one empirically determined characteristic for each polypeptide in the index. Applicants respectfully submit that the Office has failed to establish a *prima facie* case of anticipation because Yates does not describe this element of the claimed invention. *C.R. Bard*, 157 F.3d 1340 at 1349.

As with the previous rejection over Masselon et al., the Office generally cites to text in Yates but fails to show how such descriptions support the Office's conclusion and again cursorily finds the declaration by Dr. Camp inadequate. However, the cited passages fail to describe an annotated polypeptide index having at least one empirically determined characteristic for each polypeptide in the index as described and claimed in the application.

Regarding the declaration submitted by Dr. Camp under 37 C.F.R. § 1.132 as expert in the field of proteomics and mass spectrometry, a factual basis for Dr. Camp's opinion that Yates does not teach the claimed invention was provided when it stated:

Regarding Yates, this reference, similar to Masselon et al., describes the use of a database of **predicted** values based on *in silico* digestion with a site specific enzyme.

Camp Declaration at paragraph 6 (emphasis added).

The reference to "predicted values" and "*in silico* digestion" of polypeptides refers to a theoretical the process of computer generating predicted peptides. Therefore, the declaration sufficiently shows that the tryptic peptides were not empirically determined.

As described previously, the plain meaning of the claim term "empirically determined" means that any annotated polypeptide index alleged to be described in Yates should be based on factual information, observation, or direct sense experience usually as opposed to theoretical knowledge." *Webster's Third New International Dictionary, Unabridged*. Merriam-Webster, 2002. <http://unabridged.merriam-webster.com> (20 Mar. 2005). The descriptions in Yates alleged to describe the claimed invention fails to describe an empirically determined characteristic for the described databases because for both mass mapping and shotgun identification the comparison of the determined polypeptide mass is against the predicted mass of proteins in a database. For example, Yates describes mass mapping as a comparison of a determined mass with the predicted mass of a database sequence when he states:

Peptide mass mapping. A protein sequence can be verified by site-specific digestion and measurement of the peptide ions for correlation with those predicted by the sequence. Conversely, if the identity of the protein is not known the

peptide mass map can be used to search the protein database to find the sequence that best fits the mass map.

Yates, page 8, Figure 3 legend (emphasis added).

Similarly, Yates also describes shotgun identification as a comparison of a determined set of masses from a mixture with predicted masses of a database sequences to algorithmically reconstruct the identity of polypeptides in the mixture when he states:

[D]irect and automated analysis of peptide tandem mass spectra is possible with the use of computer algorithms and databases. . . . The smaller fragments are analyzed [by tandem mass spectrometry] and computer algorithms are then used to reconstruct the identities of the proteins.

Id., page 13, last sentence through page 13, line 5 (emphasis added). Moreover, Figure 8 expressly describes that the computer algorithm uses mass as the basis for search and reconstruction. There is no indication that other characteristics, including empirically determined characteristics, are searched or even included in the queried databases.

The predicted masses used in mass mapping and the algorithmic reconstruction based on predicted masses used in shotgun identification do not correspond to characteristics empirically determined. Such masses are theoretically derived because they are predicted or forecasted by a computer from an amino acid sequence and, therefore, are empirically determined. Accordingly, Yates does not describe an annotated polypeptide index containing at least one empirically determined characteristic for each of the polypeptides in the index and withdrawal of this ground of rejection is respectfully requested.

Claims 1,2, 12, 44 and 50 stand rejected under 35 U.S.C. § 102(b) as anticipated by Clauser et al. The Office alleges that Clauser et al. describes a method of identifying and characterizing proteins by mass spectrometry. The Office maintains that a peptide mass database corresponds to an annotated polypeptide index, citing page 5073, left col., lines 60-63, and Figure 2 as support. The Office further alleges that the declaration by Dr. Camp is inadequate for the same reasons provided previously.

As with the previous rejections, the Office generally cites to passages in Clauser et al. and cursorily dismisses the proffered declaration. However, the Office fails to show how such descriptions support the Office's conclusion or accord the declaration its due weight. As with the previous rejections, the cited passages fail to describe an annotated polypeptide index having at least one empirically determined characteristic for each polypeptide in the index as described and claimed in the application and teach away from the claimed polypeptide index.

Regarding the declaration submitted by Dr. Camp under 37 C.F.R. § 1.132 as expert in the field of proteomics and mass spectrometry, a factual basis for Dr. Camp's opinion that Clauser et al. does not teach the claimed invention was provided when it stated:

With respect to Clauser et al., this reference describes the use of a database constructed from a **theoretical** digest of the OWL protein sequence database. Although Clauser et al. describes using liquid chromatography to separate peptides, this information is not used as part of the identification of the proteins.

Camp Declaration at paragraph 7 (emphasis added).

The reference to "theoretical" digest of a protein sequence database refers to a speculative or non-empirical process of computer generating predicted peptides. Therefore, the declaration sufficiently shows that the peptide database was not empirically determined.

Further, and as with the previous cited art, the descriptions in Clauser et al. expressly teach away from a polypeptide index having at least one empirically determined characteristic. Clauser et al. explicitly describe that the peptide characteristics in the employed database are theoretical when he states:

Experimentally determined masses were used with MOWSE data-base searching to match theoretical peptide masses and attempt to predict protein identities.

Clauser et al., page 5073, left col., lines 60-63 (emphasis added).

The description in Clauser et al. cited as support by the Office fails to describe an empirically determined characteristic for the described databases because the search is preformed against theoretical peptide masses. Moreover, the databases shown in cited Figure 2 also fail to describe

a database containing an empirically determined characteristic since both the mass and the sequence database are deduced or theoretically determined. Because such theoretically derived masses do not constitute an empirically determined characteristic, Clauser et al. cannot anticipate the claimed invention and withdrawal of this ground of rejection is respectfully requested.

Rejections Under 35 U.S.C. § 103

Claims 1-12 and 44-50 remain rejected under 35 U.S.C. § 103(a) as obvious over Clauser et al. and Gygi et al. Claims 13-23, 51 and 52 also remain rejected under 35 U.S.C. § 103(a) as obvious over Clauser et al. and Gygi et al. For both grounds of rejections, the Office alleges that the claimed invention is obvious over the cited references because Clauser et al. does describe the generation of an annotated polypeptide index having at least one empirically determined characteristic. As with the anticipation rejection over Clauser et al., the Office relies on the passage at page 5073, left col., lines 60-63 and Figure 2 of Clauser et al. as support.

To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. In re Royka, 180 USPQ 580 (C.C.P.A. 1974); M.P.E.P. §2143.03.

Applicants respectfully submit that the Office has not established a *prima facie* case of obviousness, at least because all the steps of the claimed method for identifying a polypeptide are not taught or suggested by the cited art.

The pending claims recite comparing characteristics associated with a polypeptide to an annotated polypeptide index having at least one empirically determined characteristic for each polypeptide in the index. However, the cited references, alone or in combination, do not teach or suggest a an annotated polypeptide index having the claimed at least one empirically determined characteristic. As described previously, Clauser et al. expressly teaches away from a database containing empirically determined characteristics because Clauser et al. describes searching a database “to match theoretical peptide masses and attempt to predict protein identities.” *Id.*, page 5073, left col., lines 60-63 (emphasis added). Because Clauser et al. describes a database with theoretical masses, Clauser et al. does teach or suggest an annotated polypeptide index

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AEBERSOLD, RUDOLPH H., et al.

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having empirically determined characteristics as claimed. In the absence of a teaching or suggestion in the cited references of each element of the claimed methods, the Office has not established a *prima facie* case of obviousness of any of the claims under 35 U.S.C. § 103(a). Accordingly, Applicants respectfully request that this ground of rejection be withdrawn.


CONCLUSION

In light of the Amendments and Remarks herein, Applicant submits that the claims are in condition for allowance and respectfully request a notice to this effect. Should the Examiner have any questions, he is invited to call the undersigned attorney.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

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